

CLAIMS

1. Use of molecular markers for detection, prognosis and follow up of Parkinson's disease, wherein said molecular markers are one or more genes with altered expression pattern, or gene products thereof, said genes being selected from the group consisting of: ALDH1A1, ARPP-21, HSPA8, SKP1A, SLC18A2, SRPK2, TMEFF1, TRIM36, ADH5, PSMA3, PSMA2, PSMA5, PSMC4, HIP2, PACE4, COX6A1, PFKP, OXCT, GBE1, UQCRC2, LANCL1, TRIP15, PIK3CA, PLCL1, GNG5, GNAI1, VEGF, RHOB, NR4A2, SCL31A2, SCP2, PIGH, ARIH2, GMPR2, PP, IKBKAP, PRKACB, PTPRN2, BCAS2, IARS, PPP1R8, SEP15, TAF9, ZFP103, WRB, TMEM4, SMARCA3, FMR1, PDE6D, SGCE, AUH, SLC16A7, ATP6V1E1, UGTREL1, SEC22L1, CD9, CDH19, DUSP1, HSA6591, ACTR3, KIF2, TUBB2, ASPA, HELO1, C3orf4, CBR1, XPOT, LOC51142, NY-REN-45, SET0-2, EGLN1, EIF4EBP2, LGALS9, LOC56920, LRP6, MAN2B1, PARVA, PENK, SELPLG, SPHK1, SRRM2, ZSIG11, ITGB3BP, ITGAM, COL18A1, TM4SF9, LAMB2, HS3ST2, TSTA3, COL5A3, PALM, MYOM1, FLNB, HMBS, KRT2A, CSK, NUDC, HYPE, GAK, SIAT1, CSF1R, ICSBP1, CD22, ERCC1, DNAJB5, TRAF3, MMP9, EIF4G1, RPL36, SRPK1, CSNK1G2, RPS6KA1, JIK, LNK, INPP5D, TCOF1, NAPG, SLC19A1, ITSN1, LOC51035, PMVK, C21orf2, EFEMP2, TBL1X, APRT, SPUF, GLTSCR2, ADIR, PSCD4, CBFA2T1, CUGBP1, ING4, STAT6, ZNF239, TAL1, TAF11, MXD4, RDHL, LOC51157, LRP6, MBD3, and C9orf7.
2. Use according to claim 1 wherein said one or more genes are selected from the group consisting of: ALDH1A1, ARPP-21, HSPA8, SKP1A, SLC18A2, SRPK2, TMEFF1, TRIM36, ADH5, PSMA3, PSMA2, PSMA5, PSMC4, EGLN1, EIF4EBP2, LGALS9, LOC56920, LRP6, MAN2B1, PARVA, PENK, SELPLG, SPHK1, SRRM2, and ZSIG11.

3. A method for diagnosis, prognosis and/or follow up of Parkinson's disease comprising the use of molecular markers, wherein said molecular markers are one or more genes with altered expression pattern, or gene products thereof, said genes being selected from the group consisting of: ALDH1A1, ARPP-21, HSPA8, 5 SKP1A, SLC18A2, SRPK2, TMEFF1, TRIM36, ADH5, PSMA3, PSMA2, PSMA5, PSMC4, HIP2, PACE4, COX6A1, PFKP, OXCT, GBE1, UQCRC2, LANCL1, TRIP15, PIK3CA, PLCL1, GNG5, GNAI1, VEGF, RHOB, NR4A2, SCL31A2, SCP2, PIGH, ARIH2, GMPR2, PP, IKBKAP, PRKACB, PTPRN2, BCAS2, IARS, PPP1R8, SEP15, TAF9, ZFP103, WRB, TMEM4, SMARCA3, 10 FMR1, PDE6D, SGCE, AUH, SLC16A7, ATP6V1E1, UGTREL1, SEC22L1, CD9, CDH19, DUSP1, HSA6591, ACTR3, KIF2, TUBB2, ASPA, HELO1, C3orf4, CBR1, XPOT, LOC51142, NY-REN-45, SET0-2, EGLN1, EIF4EBP2, LGALS9, LOC56920, LRP6, MAN2B1, PARVA, PENK, SELPLG, SPHK1, SRRM2, ZSIG11, ITGB3BP, ITGAM, COL18A1, TM4SF9, LAMB2, HS3ST2, TSTA3, 15 COL5A3, PALM, MYOM1, FLNB, HMBS, KRT2A, CSK, NUDC, HYPE, GAK, SIAT1, CSF1R, ICSBP1, CD22, ERCC1, DNAJB5, TRAF3, MMP9, EIF4G1, RPL36, SRPK1, CSNK1G2, RPS6KA1, JIK, LNK, INPP5D, TCOF1, NAPG, SLC19A1, ITSN1, LOC51035, PMVK, C21orf2, EFEMP2, TBL1X, APRT, SPUF, GLTSCR2, ADIR, PSCD4, CBFA2T1, CUGBP1, ING4, STAT6, ZNF239, TAL1, 20 TAF11, MXD4, RDHL, LOC51157, LRP6, MBD3, and C9orf7.

4. A method according to claim 3, wherein said molecular markers are one or more genes selected from the group consisting of: ALDH1A1, ARPP-21, HSPA8, SKP1A, SLC18A2, SRPK2, TMEFF1, TRIM36, ADH5, PSMA3, PSMA2, PSMA5, PSMC4, EGLN1, EIF4EBP2, LGALS9, LOC56920, LRP6, MAN2B1, 25 PARVA, PENK, SELPLG, SPHK1, SRRM2, and ZSIG11.

5. A method according to claim 3, which comprises detecting a decreased level of expression of one or more genes selected from the group consisting of: ALDH1A1, ARPP-21, HSPA8, SKP1A, SLC18A2, SRPK2, TMEFF1, TRIM36, ADH5, PSMA3, PSMA2, PSMA5, PSMC4, HIP2, PACE4, COX6A1, PFKP,

OXCT, GBE1, UQCRC2, LANCL1, TRIP15, PIK3CA, PLCL1, GNG5, GNAI1, VEGF, RHOB, NR4A2, SCL31A2, SCP2, PIGH, ARIH2, GMPR2, PP, IKBKAP, PRKACB, PTPRN2, BCAS2, IARS, PPP1R8, SEP15, TAF9, ZFP103, WRB, TMEM4, SMARCA3, FMR1, PDE6D, SGCE, AUH, SLC16A7, ATP6V1E1, 5 UGTREL1, SEC22L1, CD9, CDH19, DUSP1, HSA6591, ACTR3, KIF2, TUBB2, ASPA, HELO1, C3orf4, CBR1, XPOT, LOC51142, NY-REN-45, SET0-2, and/or an increased level of expression of one or more genes selected from the group consisting of: EGLN1, EIF4EBP2, LGALS9, LOC56920, LRP6, MAN2B1, PARVA, PENK, SELPLG, SPHK1, SRRM2, ZSIG11, ITGB3BP, ITGAM, 10 COL18A1, TM4SF9, LAMB2, HS3ST2, TSTA3, COL5A3, PALM, MYOM1, FLNB, HMBS, KRT2A, CSK, NUDC, HYPE, GAK, SIAT1, CSF1R, ICSBP1, CD22, ERCC1, DNAJB5, TRAF3, MMP9, EIF4G1, RPL36, SRPK1, CSNK1G2, RPS6KA1, JIK, LNK, INPP5D, TCOF1, NAPG, SLC19A1, ITSN1, LOC51035, PMVK, C21orf2, EFEMP2, TBL1X, APRT, SPUF, GLTSCR2, ADIR, PSCD4, 15 CBFA2T1, CUGBP1, ING4, STAT6, ZNF239, TAL1, TAF11, MXD4, RDHL, LOC51157, LRP6, MBD3, and C9orf7.

6. A method according to claim 5, which comprises detecting a decreased level of expression of one or more genes selected from the group consisting of: ALDH1A1, ARPP-21, HSPA8, SKP1A, SLC18A2, SRPK2, TMEFF1, TRIM36, 20 ADH5, PSMA3, PSMA2, PSMA5, PSMC4, and/or an increased level of expression of one or more genes selected from the group consisting of: EGLN1, EIF4EBP2, LGALS9, LOC56920, LRP6, MAN2B1, PARVA, PENK, SELPLG, SPHK1, SRRM2, ZSIG11.

7. A method for diagnosing occurrence of Parkinson's disease in an individual exhibiting Parkinsonian-like symptoms, comprising detecting in a sample obtained from said individual a decreased level of expression of one or more genes selected from the group consisting of: ALDH1A1, ARPP-21, HSPA8, SKP1A, SLC18A2, SRPK2, TMEFF1, TRIM36, ADH5, PSMA3, PSMA2, PSMA5, PSMC4, HIP2, PACE4, COX6A1, PFKP, OXCT, GBE1, UQCRC2, LANCL1, TRIP15, PIK3CA, 25

PLCL1, GNG5, GNAI1, VEGF, RHOB, NR4A2, SCL31A2, SCP2, PIGH, ARIH2, GMPR2, PP, IKBKAP, PRKACB, PTPRN2, BCAS2, IARS, PPP1R8, SEP15, TAF9, ZFP103, WRB, TMEM4, SMARCA3, FMR1, PDE6D, SGCE, AUH, SLC16A7, ATP6V1E1, UGTREL1, SEC22L1, CD9, CDH19, DUSP1, HSA6591, 5 ACTR3, KIF2, TUBB2, ASPA, HELO1, C3orf4, CBR1, XPOT, LOC51142, NY-REN-45, and SET0-2, and/or an increased level of expression of one or more genes selected from the group consisting of: EGLN1, EIF4EBP2, LGALS9, LOC56920, LRP6, MAN2B1, PARVA, PENK, SELPLG, SPHK1, SRRM2, ZSIG11, ITGB3BP, ITGAM, COL18A1, TM4SF9, LAMB2, HS3ST2, TSTA3, COL5A3, 10 PALM, MYOM1, FLNB, HMBS, KRT2A, CSK, NUDC, HYPE, GAK, SIAT1, CSF1R, ICSBP1, CD22, ERCC1, DNAJB5, TRAF3, MMP9, EIF4G1, RPL36, SRPK1, CSNK1G2, RPS6KA1, JIK, LNK, INPP5D, TCOF1, NAPG, SLC19A1, ITSN1, LOC51035, PMVK, C21orf2, EFEMP2, TBL1X, APRT, SPUF, GLTSCR2, ADIR, PSCD4, CBFA2T1, CUGBP1, ING4, STAT6, ZNF239, TAL1, 15 TAF11, MXD4, RDHL, LOC51157, LRP6, MBD3, and C9orf7, wherein said decreased and/or increased level of expression of said genes is diagnostic of Parkinson's disease.

8. A method according to claim 7 comprising detecting a decreased level of expression of one or more genes selected from the group consisting of: ALDH1A1, 20 ARPP-21, HSPA8, SKP1A, SLC18A2, SRPK2, TMEFF1, TRIM36, ADH5, PSMA3, PSMA2, PSMA5, and PSMC4, and/or an increased level of expression of one or more genes selected from the group consisting of: EGLN1, EIF4EBP2, LGALS9, LOC56920, LRP6, MAN2B1, PARVA, PENK, SELPLG, SPHK1, SRRM2, and ZSIG11.

25 9. A method according to claim 7 or 8, wherein said sample is blood, serum or biopsy of skin from the tested individual.

10. The method according to any one of claims 7 to 9, which comprises detecting a gene product expressed by said gene and the gene product is a protein expressed by the gene or RNA transcribed from the gene, or both.

11. The method according to claim 10, wherein said detection comprises 5 assaying for the presence of a protein expressed by the gene by contacting the sample with an antibody, or a fragment thereof, that binds to the protein.

12. The method according to claim 10, which comprises detection in said sample of decreased or increased levels of RNA transcripts.

13. The method according to claim 12, wherein detection of the RNA transcripts 10 is carried out by a method selected from the group consisting of Northern blots, RNase protection assays (RPA), nucleic acid probe arrays, real-time quantitative reverse-transcription PCR (RT-PCR), dot blot assays and in-situ hybridization.

14. A method for screening for an agent useful for treating Parkinson's disease, which comprises identifying an agent that upregulates the expression of one or more 15 genes selected from the group consisting of ALDH1A1, ARPP-21, HSPA8, SKP1A, SLC18A2, SRPK2, TMEFF1, TRIM36, ADH5, PSMA3, PSMA2, PSMA5, PSMC4, HIP2, PACE4, COX6A1, PFKP, OXCT, GBE1, UQCRC2, LANCL1, TRIP15, PIK3CA, PLCL1, GNG5, GNAI1, VEGF, RHOB, NR4A2, SCL31A2, SCP2, PIGH, ARIH2, GMPR2, PP, IKBKAP, PRKACB, PTPRN2, 20 BCAS2, IARS, PPP1R8, SEP15, TAF9, ZFP103, WRB, TMEM4, SMARCA3, FMR1, PDE6D, SGCE, AUH, SLC16A7, ATP6V1E1, UGTREL1, SEC22L1, CD9, CDH19, DUSP1, HSA6591, ACTR3, KIF2, TUBB2, ASPA, HELO1, C3orf4, CBR1, XPOT, LOC51142, NY-REN-45, and SET0-2, or down-regulates the expression of one or more genes selected from the group consisting of: EGLN1, 25 EIF4EBP2, LGALS9, LOC56920, LRP6, MAN2B1, PARVA, PENK, SELPLG, SPHK1, SRRM2, ZSIG11, ITGB3BP, ITGAM, COL18A1, TM4SF9, LAMB2, HS3ST2, TSTA3, COL5A3, PALM, MYOM1, FLNB, HMBS, KRT2A, CSK, NUDC, HYPE, GAK, SIAT1, CSF1R, ICSBP1, CD22, ERCCI, DNAJB5, TRAF3,

MMP9, EIF4G1, RPL36, SRPK1, CSNK1G2, RPS6KA1, JIK, LNK, INPP5D, TCOF1, NAPG, SLC19A1, ITSN1, LOC51035, PMVK, C21orf2, EFEMP2, TBL1X, APRT, SPUF, GLTSCR2, ADIR, PSCD4, CBFA2T1, CUGBP1, ING4, STAT6, ZNF239, TAL1, TAF11, MXD4, RDHL, LOC51157, LRP6, MBD3, and 5 C9orf7.

15. A method according to claim 14 which comprises identifying an agent that upregulates the expression of one or more genes selected from the group consisting of: ALDH1A1, ARPP-21, HSPA8, SKP1A, SLC18A2, SRPK2, TMEFF1, TRIM36, ADH5, PSMA3, PSMA2, PSMA5, PSMC4, or down-regulates the 10 expression of one or more genes selected from the group consisting of: EGLN1, EIF4EBP2, LGALS9, LOC56920, LRP6, MAN2B1, PARVA, PENK, SELPLG, SPHK1, SRRM2, ZSIG11.